APPENDIX 1: MARKED-UP VERSION OF AMENDMENTS

IN THE SPECIFICATION:

Specification, at page 1, the first sentence of the first paragraph (under "RELATED APPLICATIONS"):

-- This is a Divisional Application of allowed United States Patent Application No. 09/224,014, which is a Continuing Application of PCT/GB97/02857, filed October 17, 1997 and claiming priority to Great Britain Patent Application No. 9621680.9, filed October 17, 1996, and Great Britain Patent Application No. 9624457.9, filed November 25, 1996. --

IN THE CLAIMS:

-- 20. (New) An infection and transduction competent, lentivirus-based retroviral vector particle comprising a genome, gag, pol, an envelope protein, and optionally a rev protein or functional equivalents thereof, wherein the particle lacks all functional lentiviral auxiliary gene products other than the optionally rev protein or functional equivalents thereof.

21. (New) An infection and transduction competent, lentivirus-based retroviral vector particle comprising a genome, gag, pol, and an envelope protein, wherein the particle lacks all functional lentiviral auxiliary gene products; or the particle lacks all functional lentiviral auxiliary gene products, except a rev protein or functional equivalents thereof.

22. (New) The retroviral vector particle according to claim 20 or 21 wherein the retroviral vector particle further comprises a nucleic acid sequence which encodes one or more genes of interest.

23. (New) The retroviral vector particle according to claim 22 wherein the gene of interest encodes a therapeutic protein.

24. (New) An isolated cell comprising the retroviral vector particle of claim 23.

25. (New) A composition comprising the retroviral vector particle of claim 22 and a carrier.

26. (New) A composition comprising the retroviral vector particle of claim 23 and a carrier.

27. (New) A method for expressing a gene of interest or replicating a nucleic acid molecule therefor comprising contacting a cell with the retroviral vector particle of claim 22.

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28. (New) A method for expressing a gene of interest comprising introducing a gene of interest into a cell by contacting said cell with the retroviral vector particle of claim 22.

29. (New) A retroviral vector production system for producing the infection and transduction competent, lentivirus-based retroviral vector particle according to claim 20, which system comprises nucleic acid sequence(s) encoding the genome of the retroviral vector particle, gag, pol, and the envelope protein, and optionally the rev protein or functional equivalents thereof, wherein all lentiviral auxiliary genes, or all lentiviral auxiliary genes except the optionally present *rev* or functional equivalents thereof, are absent or are disrupted, whereby functional auxiliary proteins encoded by said auxiliary genes are not expressed in the system.

30. (New) A retroviral vector production system for producing infection and transduction competent, lentivirus-based vector particle according to claim 21, which system comprises nucleic acid sequence(s) encoding the genome of the vector particle, gag, pol, and an envelope protein, or the genome of the vector particle, gag , pol, an envelope protein, and a rev protein or functional equivalents thereof, wherein all lentiviral auxiliary genes, or all lentiviral auxiliary genes except *rev* or functional equivalents thereof, are absent or are disrupted, whereby functional auxiliary proteins encoded by said auxiliary genes are not expressed in the system.

31. (New) The retroviral vector production system according to claim 29 or 30, wherein the nucleic acid sequence encoding the genome of the vector further comprises one or more genes of interest.

32. (New) The retroviral vector production system according to claim 31, wherein the gene of interest encodes a therapeutic protein.

33. (New) The retroviral vector production system according to claim 29 or 30, wherein the nucleic acid sequence(s) include three DNA constructs which encode: the genome of the vector particle, gag and pol proteins, and the envelope protein, respectively.

34. (New) The retroviral vector production system according to claim 29 or 30, wherein the nucleic acid sequence comprises *rev* or functional equivalents thereof and RRE sequences.

35. (New) A retroviral vector particle produced by the system according to claim 29 or 30, wherein the nucleic acid sequence encoding the genome of the vector particle further comprises one or more genes of interest.

36. (New) A method for expressing a gene product comprising introducing a gene of interest into a cell by contacting said cell with the retroviral vector particle according to claim 35.

37 (New) A composition comprising the retroviral vector particle according to claim 35, in a carrier.

38. (New) An isolated cell comprising the retroviral particle of claim 35 on or in the cell.

39. (New) The retroviral vector particle according to claim 35, wherein the gene of interest encodes a therapeutic protein.

40. (New) A method for expressing a gene product comprising introducing a gene of interest into a cell by contacting said cell with the retroviral vector particle according to claim 39.

41. (New) An isolated cell comprising the retroviral particle of claim 39 on or in the cell.

42. (New) An isolated cell comprising the retroviral particle of claim 22 on or in the cell.

43. (New) The retroviral vector particle of any one of claims 20 or 21, wherein the rev protein or functional equivalents thereof is present.

44. (New) The retroviral vector particle of claim 22, wherein the rev protein or functional equivalents thereof is present.

45. (New) The retroviral vector particle of claim 23, wherein the rev protein or functional equivalents thereof is present.

46. (New) The retroviral vector particle of claim 35, wherein the rev protein or functional equivalents thereof is present.

47. (New) The retroviral production system of any one of claims 29 or 30 wherein the genome includes an operable promoter.

48. (New) The retroviral production system of claim 47 wherein the promoter is a non-retroviral promoter.

49. (New) A set of nucleic acid sequences encoding the components of the infection and transduction competent, lentivirus-basedvector particle according to any one of claims 20 or 21, comprising: a first DNA construct which encodes the genome of the vector particle, a second

DNA construct which encodes gag and pol proteins, and a third DNA construct which encodes an envelope protein, wherein: one of the DNA constructs optionally encodes a rev protein or functional equivalents thereof; and all other lentiviral auxiliary gene products are absent from the retroviral vector particle and producer cells in which the sequences are expressed, and lentiviral auxiliary genes encoding said other lentiviral auxiliary gene products are absent from or disrupted in the set of sequences.

50. (New) The set of nucleic acid sequences of claim 49, wherein *rev* or functional equivalents thereof is present.

51. (New) The set of nucleic acid sequences of claim 49 which further comprises one or more genes of interest.

52. (New) The set of nucleic acid sequences of claim 49 wherein the genome includes an operable promoter.

53. (New) The set of nucleic acid sequences of claim 52 wherein the promoter is a non-retroviral promoter.

54. (New) A method for producing the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 or 21, comprising coexpressing in a retroviral producer cell nucleic acid sequence(s) encoding the genome of the vector particle, gag and pol proteins, and an envelope protein, and, optionally a rev protein or functional equivalents thereof; wherein one of the nucleic acid sequence(s) optionally encodes a rev protein or functional equivalents thereof; and all other lentiviral auxiliary gene products are absent from the retroviral vector particle and producer cells in which the sequence(s) are expressed, and lentiviral auxiliary genes encoding said other lentiviral auxiliary gene products are absent from or disrupted in the sequence(s).

55. (New) A method for producing the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 or 21, comprising coexpressing in a retroviral producer cell nucleic acid sequence(s) encoding the genome of the vector particle, gag and pol proteins, and an envelope protein; wherein all lentiviral auxiliary gene products are absent from the retroviral vector particle and producer cells in which the sequence(s) are expressed, and lentiviral auxiliary genes encoding said lentiviral auxiliary gene products are absent from or disrupted in the sequence(s).

56. (New) A method for producing the infection and transduction competent, lentivirus-based, replication defective vector particle according to claim 20 or 21, consisting essentially of coexpressing in a retroviral producer cell nucleic acid sequence(s) encoding the genome of the vector particles, gag and pol proteins, and an envelope protein.

57. (New) The method of claim 54 wherein the nucleic acid sequence(s) include one or more genes of interest.

58. (New) The method of claim 55 wherein the nucleic acid sequence(s) include one or more genes of interest.

59. (New) The method of claim 56 wherein the nucleic acid sequence(s) include one or more genes of interest.

60. (New) The method of claim 54 wherein the coexpressing is of: a first DNA construct which encodes the genome of the vector particles, a second DNA construct which encodes gag and pol proteins, and a third DNA construct which encodes the envelope protein, wherein one of the DNA constructs optionally encodes a rev protein or functional equivalents thereof.

61. (New) The method of claim 55 wherein the coexpressing is of: a first DNA construct which encodes the genome of the vector particles, a second DNA construct which encodes gag and pol proteins, and a third DNA construct which encodes the envelope protein.

62. (New) The method of claim 56 wherein the coexpressing is of: a first DNA construct which encodes the genome of the vector particles, a second DNA construct which encodes gag and pol proteins, and a third DNA construct which encodes the envelope protein, wherein one of the DNA constructs optionally encodes a rev protein or functional equivalents thereof.

63. (New) The method of claim 54 wherein the coexpressing includes expressing a DNA construct which encodes gag and pol proteins independent of auxiliary genes.

64. (New) The method of claims 56 wherein the coexpressing includes expressing a DNA construct which encodes gag and pol proteins independent of auxiliary genes.

65. (New) The method of claim 54 wherein *rev* is present or a rev protein or functional equivalents thereof is expressed.

66. (New) The method of claim 56 wherein *rev* is present or a rev protein or functional equivalents thereof is expressed.

67. (New) The method of claim 54 wherein the nucleic acid sequence(s) further includes one or more genes of interest.

68. (New) The method of claim 55 wherein the nucleic acid sequence(s) further includes one or more genes of interest.

69. (New) The method of claim 56 wherein the nucleic acid sequence(s) further consists essentially of one or more genes of interest.

70. (New) The method of claim 54 wherein the genome further includes an operable promoter.

71. (New) The method of claim 55 wherein the genome further includes an operable promoter.

72. (New) The method of claim 56 wherein the genome further consists essentially of an operable promoter.

73. (New) The method of claim 54 wherein the promoter is a non-retroviral promoter.

74. (New) The method of claim 55 wherein the promoter is a non-retroviral promoter.

75. (New) The method of claim 56 wherein the promoter is a non-retroviral promoter.

76. (New) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 54, wherein the particle lacks all functional lentiviral auxiliary gene products other than the optionally present rev protein or functional equivalents thereof.

77. (New) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 55, wherein the particle lacks all functional lentiviral auxiliary gene products other than the optionally present rev protein or functional equivalents thereof.

78. (New) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 56, wherein the particle lacks all functional lentiviral auxiliary gene products other than the optionally present rev protein or functional equivalents thereof.

79. (New) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 57, wherein the particle lacks all functional lentiviral auxiliary gene products other than the optionally present rev protein or functional equivalents thereof.

80. (New) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 58, wherein the particle lacks all functional lentiviral auxiliary gene products other than the optionally present rev protein or functional equivalents thereof.

81. (New) An infection and transduction competent, lentivirus-based, replication defective vector particle produced by the method of claim 59, wherein the particle lacks all functional lentiviral auxiliary gene products other than the optionally present rev protein or functional equivalents thereof.

82. (New) An isolated nucleic acid sequence encoding the components of the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 or 21, comprising DNA construct(s) which encode the genome of the vector particle, gag and pol proteins, and an envelope protein, wherein, the nucleic acid sequence produces the lentivirus-based, replication defective vector particle, and, wherein: the DNA construct(s) optionally encode a rev protein or functional equivalents thereof; and all other functional auxiliary gene products are absent from the retroviral vector particle and producer cells in which the nucleic acid sequence is expressed, and are also absent from or disrupted in the nucleic acid sequence.

83. (New) Isolated nucleic acid sequence(s) encoding the components of the infection and transduction competent, lentivirus-based, replication defective vector particle as claimed in claim 20 or 21, comprising construct(s) which encode the genome of the vector particle, gag and pol proteins, and an envelope protein, wherein all functional auxiliary gene products, or all functional auxiliary gene products except rev protein or functional equivalents thereof, are absent from the retroviral vector particle and producer cells in which the nucleic acid sequence(s) is/are expressed and are absent from or disrupted in the sequence(s).

84. (New) Isolated nucleic acid sequence(s) encoding the components of the infection and transduction competent, lentivirus-based vector particle of claim 20 or 21, consisting essentially of construct(s) which encode(s) the RNA genome of the vector particle,

gag and pol proteins, and an envelope protein, wherein the construct(s) optionally encode(s) rev or functional equivalents thereof.

85. (New) The retroviral vector production system wherein according to claim 29 or 30 wherein the retroviral vector particle is based on HIV-1 and auxiliary genes *vpu, vpr, vif, tat* and *nef* are absent or are disrupted.

86. (New) The retroviral particle of claim 20 or 21 which is based on HIV-1 and auxiliary genes *vpu, vpr, vif, tat* and *nef* are absent or are disrupted.

87. (New) The retroviral particle of claim 20 or 21 which is based on HIV-1 and auxiliary genes *vpu, vpr, vif, tat, rev* and *nef* are absent or are disrupted.

88. (New) A retroviral particle according to claim 20 or 21 wherein the envelope protein is VSV-G.

89. (New) The retroviral vector production system wherein according to claim 29 or 30 wherein rev or functional equivalents thereof is present as a constitutive transport element (CTE).

90. (New) The retroviral particle of claim 20 or 21 wherein rev or functional equivalents thereof is present as a constitutive transport element (CTE). --

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